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Heterocyclic dicyanovinyl derivatives: synthesis and evaluation of the chemosensory ability in aqueous solution

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Abstract: Two novel dicyanovinyl derivatives **3a**-**b** were synthesized in moderate to good yields through a Knoevenagel reaction of the corresponding aldehyde precursors and malononitrile. The photophysical properties of the new push-pull systems were studied by UV-vis and fluorescence spectroscopy in acetonitrile. The evaluation of the compounds as colorimetric chemosensors was carried out by performing spectrophotometric titrations in acetonitrile and acetonitrile/water in the presence of relevant organic and inorganic anions, and of alkaline, alkaline-earth and transition metal cations. The benzoindole derivative exhibited great selectivity for the cyanide anion over other anions in acetonitrile/water (8:2) solution showing a distinct color change from colorless to yellow.

Keywords: Knoevenagel reaction; benzofuran; benzoindole; push-pull dicyanovinyl heterocyclic compounds; colorimetric sensors; aqueous media.

1. Introduction

The cyanide anion is well known due to its toxicity to the environment and to mammals, leading to convulsions, loss of consciousness, and eventual death. It is lethal to humans in concentrations in the range of 0.5-3.5 mg per Kg of body weight. In addition to being found in many foods and plants, cyanides are used industrially in the synthesis of organic chemicals, polymers, metallurgy as well as in gold mining [1].

Consequently, selective detection and quantification of cyanide is very important and it has been the object of increasing investigation. A large number of fluorimetric and/or colorimetric chemosensors as well as dosimeters, capable of detecting this anion in organic solvents as well as in aqueous mixtures have been reported during the last decade. Even so, the majority suffer from several drawbacks such as difficult synthesis, poor selectivity, only work in an organic media and the use of instrumentation is required [2]. Therefore, the research on versatile and tunable chemosensors capable of selective and sensitive colorimetric sensing of the cyanide anion, especially in mixed aqueous solutions, is still a challenge [3].

Having in mind the work developed in our research group concerning push-pull dicyanovinyl derivatives for several optical applications (SHG and TPA NLOphores) [4], we report in this work, the synthesis, characterization and evaluation of the photophysical properties and the chemosensory

ability of novel optical chemosensors based on benzofuran and benzoindole systems functionalized with the dicyanovinyl group.

2. Experimental

2.1. General procedure for the synthesis of dicyanovinyl derivatives 3a-b

A solution of aldehyde **2a** or **2b** (0.37 mmol), malononitrile **1** (0.37 mmol) and piperidine (1 drop) in ethanol (5 mL) was heated at reflux for 5 h. After this time the solvent was evaporated and the resulting crude products were purified by column chromatography (silica gel, petroleum ether /dichloromethane (1:1)).

2.1.1. 2-((1H-Benzo[g]indol-3-yl)methylene)malononitrile **3a**

Compound **3a** was obtained as a light yellow solid (40 mg, 65%). Mp > 300 °C. UV-vis (acetonitrile): λ_{max} nm (log ε) 374 (4.40). ^{1}H NMR (DMSO-d_6): δ= 7.52 (dt, J = 8.0 and 1.2 Hz, 1H, H-7), 7.64 (dt, J = 8.0 and 1.2 Hz, 1H, H-8), 7.74 (d, J = 8.8 Hz, 1H, H-5), 8.0 (d, J = 8.0 Hz, 1H, H-6), 8.11 (d, J = 8.8 Hz, 1H, H-4), 8.41 (d, J = 8.4 Hz, 1H, H-9), 8.49 (s, 1H, H-2), 8.82 (s, 1H, CH=C), 13.55 (s, 1H, NH) ppm. ^{13}C NMR (DMSO-d_6): δ= 70.91 (C-(CN)$_2$), 112.38 (C-3a), 115.64 (C≡N), 115.71 (C≡N), 118.18 (C-4), 120.76 (C-9), 121.61 (C-9a), 123.28 (C-5), 123.39 (C-3), 125.14 (C-7), 126.57 (C-8), 128.62 (C-6), 129.91 (C-2), 130.70 (C-5a), 131.17 (C-3b), 153.05 (CH=C) ppm.

2.1.2. 2-((Benzofuran-2-yl)methylene)malononitrile **3b**

Compound **3b** was obtained as a yellow solid (49 mg, 74%). M.p. 170.9-171.5 °C. UV-vis (acetonitrile): λ_{max} nm (log ε) 361 (4.61). ^{1}H NMR (DMSO-d_6): δ= 7.40 (dt, J = 8.0 and 1.2 Hz, 1H, H-5), 7.60 (dt, J = 8.4 and 1.2 Hz, 1H, H-6), 7.70 (dd, J = 8.8 and 0.8 Hz, 1H, H-7), 7.83 (s, 1H, H-3), 7.88 (dd, J = 8.0 and 1.2 Hz, 1H, H-4), 8.48 (s, 1H, CH=C) ppm. ^{13}C NMR (DMSO-d_6): δ= 78.67 (C-(CN)$_2$), 111.99 (C-7), 113.07 (C≡N), 114.35 (C≡N), 121.34 (C-3), 123.92 (C-4), 124.70 (C-5), 127.09 (C-3a), 130.25 (C-6), 145.44 (CH=C), 148.98 (C-2), 156.14 (C-7a) ppm.

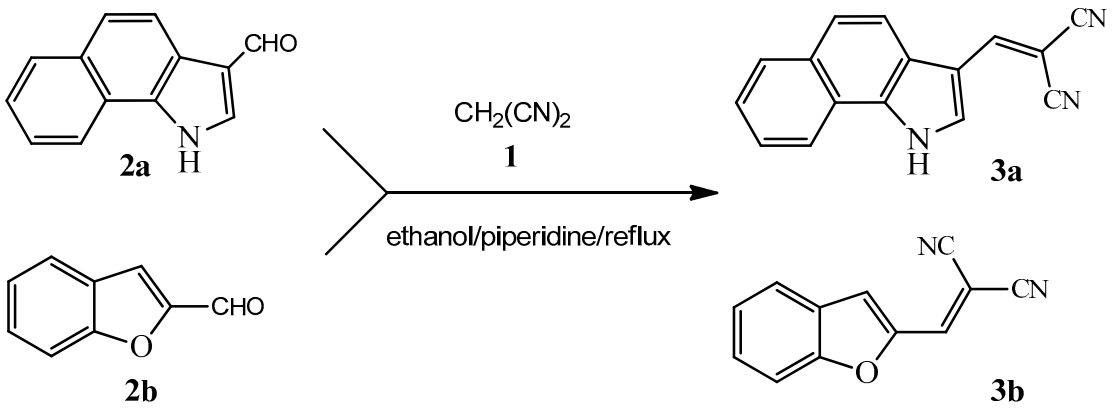
2.2. Spectrophotometric titrations of compounds 3a-b

UV–visible absorption spectra (250–650 nm) were obtained using a Shimadzu UV/2501PC spectrophotometer. Fluorescence spectra were collected using a FluoroMax-4 spectrofluorometer. The relative fluorescence quantum yields were determined by using 10^{-6} M solution of Rhodamine 6G in ethanol as standard (Φ_F = 0.95) [5]. Organic solvents used in the spectroscopic studies were of spectroscopic grade. Solutions of derivatives **3a**-**b** (*ca.* 1.0 × 10^{-5} M) and of the ions under study (ca. 1.0 × 10^{-2} and 1.0 × 10^{-3} M) were prepared in UV-grade acetonitrile or acetonitrile/water (8:2). Titrations of the compounds **3a**-**b** in the presence of relevant organic and inorganic anions (AcO^-, F^-, Cl^-, Br^-, CN^-, NO_3^-, BzO^-, $H_2PO_4^-$, HSO_4^-), and of alkaline, alkaline-earth and transition metal cations (Cu^{2+}, Cd^{2+}, Pd^{2+}, Ni^{2+}, Hg^{2+}, Zn^{2+}, Fe^{2+}, Fe^{3+} and Cr^{3+}) was performed by the sequential addition of the ion stock solution to the dicyanovinyl solution, in a 10 mm path length quartz cuvette and absorption emission spectra were measured by excitation at the wavelength of maximum absorption for each compound, with a 2 nm slit.

3. Results and discussion

3.1. Synthesis and characterization

Dicyanovinyl **3a**-**b** were synthesized in moderate to good yields (65-74 %), by a Knoevenagel reaction between malononitrile **1** and aldehydes **2a**-**b**. The new compounds were completely characterized by the usual spectroscopic techniques (Scheme 1, Table 1).



Scheme 1. Synthesis of dicyanovinyl derivatives **3a**-**b**.

The absorption and emission spectra of compounds **3a**-**b** were measured in acetonitrile solutions and showed intense lowest energy charge-transfer absorption bands in the UV-visible region between 361-374 nm (absorption). Both compounds were very weakly fluorescent, with wavelengths of maximum emission close to 405-528 nm and with relative fluorescence quantum yields in the order of 0.005.

Table 1. Yields, UV-visible absorption and emission data for dicyanovinyls **3a**-**b** in acetonitrile solution.

		Absorption		Emission		
	η(%)	**λ_{max} (nm)**	**log ε**	**λ_{em} (nm)**	**Stokes' shift (nm)**	**Φ_{Flu}**
3a	65	374	4.40	528	154	0.006
3b	74	361	4.61	405	44	0.005

3.2. Spectrophotometric titrations of dicyanovinyl derivatives 3a-b with anions and metallic ions

Evaluation of new dicyanovinyl **3a**-**b** (10^{-5} M) as colorimetric chemosensors were carried out in ACN and ACN/H_2O solutions, in the presence of several ions (AcO^-, F^-, Cl^-, Br^-, CN^-, NO_3^-, BzO^-, $H_2PO_4^-$, HSO_4^-, Cu^{2+}, Cd^{2+}, Pd^{2+}, Ni^{2+}, Hg^{2+}, Zn^{2+}, Fe^{2+}, Fe^{3+} and Cr^{3+}) with biological, environmental and analytical relevance.

Preliminary tests were carried out by addition of up to 50 equiv of each ion to the solutions of dicyanovinyls **3a-b** in ACN and in aqueous mixture ACN/H_2O (8:2), revealing that only compound **3a** exhibited chemosensor ability.

It was found that **3a** displayed a marked colour change, from colourless to yellow, upon interaction with AcO, F^-, CN^-, BzO^- and $H_2PO_4^-$ in acetonitrile solution. Moreover, **3a** showed selectivity for the cyanide ion in aqueous mixture displaying the same colour change (Figure 1).

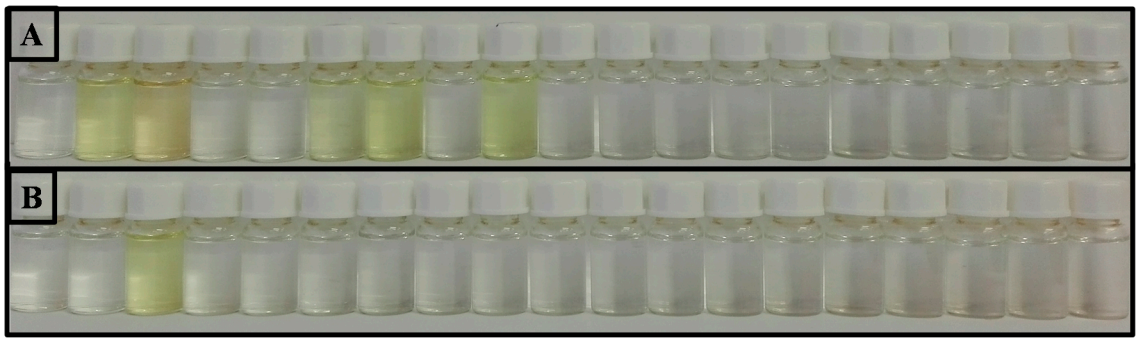


Figure 1. Colour changes of compound **3a** (10^{-4} M in A: ACN, B: ACN/H_2O (8:2)) in the presence of 50 equiv. of AcO^-, CN^-, HSO_4^-, NO_3^-, $H_2PO_4^-$, F^-, Cl^-, BzO^-, Cu^{2+}, Pd^{2+}, Zn^{2+}, Fe^{2+}, Hg^{2+}, Fe^{3+}, Co^{2+}, Ca^{2+}, Na^+ and Ni^{2+} (in the form of tetrafluorborate or perchlorate salts).

Considering these preliminary results, spectrophotometric titration of compound **3a** in ACN with these selected ions were undertaken. Titration with CN^- revealed a trend in the UV-Vis spectra, the intensity of the longest wavelength absorption band at 373 nm decreased progressively upon addition of the anion, with the simultaneous growth of a new red-shifted absorption band located at 424 nm (Figure 2). It can be seen that a very small amount of cyanide ion (0.3 equiv) caused large changes in the absorption spectrum and a drastic color change in the solution of compound **3a**.

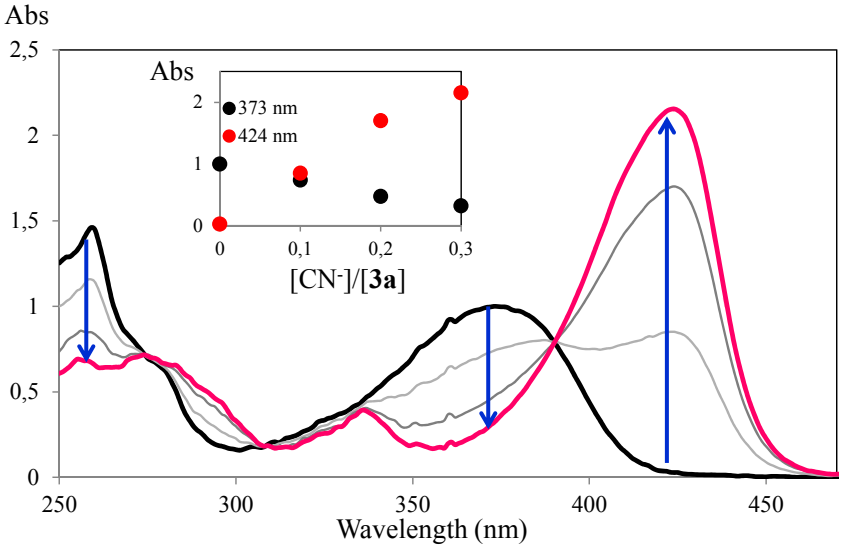


Figure 2. Spectrophotometric titrations of compound **3a** with addition of increasing amounts of CN^- in ACN. The inset represents the normalized absorption ([**3a**] = $1x10^{-5}$ M, T = 298 K).

Compound **3a**, in the titration with F^-, AcO^-, $H_2PO_4^-$ and BzO^-, revealed the same trend observed in the titration with cyanide ion (Figure 3). In the titration with F^- 0.4 equiv were used, 1 equiv was needed for titration with AcO^-, and 5 equiv for the titration with $H_2PO_4^-$ and BzO^-. Thus, although not selective, compound **3a** in acetonitrile was more sensitive to the presence of cyanide ion, considering that only 0.3 equiv of the cyanide ion were required for the visible colour change.

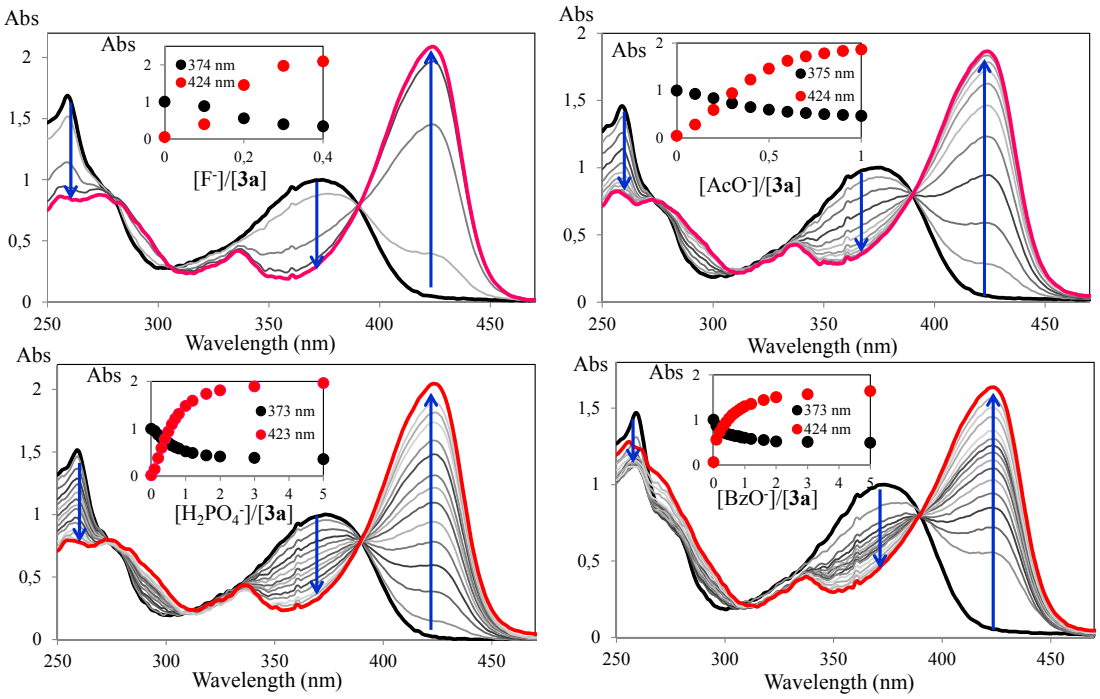


Figure 3. Spectrophotometric titration of **3a** with addition of increasing amounts of F^-, AcO^-, $H_2PO_4^-$ and BzO^- in ACN. The inset represents the normalized absorption a 373 nm ([**3a**] = 1x10^{-5} M, T = 298 K).

Spectrophotometric titrations of compound **3a** in ACN/H_2O (8:2) confirmed the preliminary sensing results, with compound **3a** being selective for the cyanide ion although it required a larger amount of ion to achieve a similar colour change (70 equiv), when compared to the titration in ACN. In Figure 4 it can be seen that there was a gradual decrease in absorption intensity upon addition of the cyanide ion, accompanied by a red-shift with the formation of a new band at 417 nm.

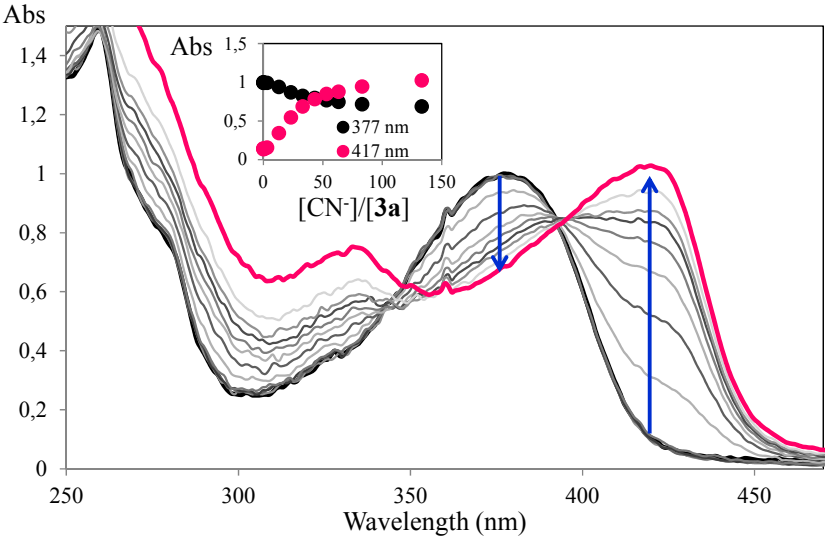


Figure 4. Spectrophotometric titration of compound **3a** with addition of increasing amounts of CN^- in ACN/H_2O (8:2). The inset represents the normalized emission ([**3a**] = 1x10^{-5} M, T = 298 K).

4. Conclusions

The synthesis of new dicyanovinyls **3a**-**b** was achieved in moderate to good yields by a simple experimental procedure. The sensory ability was evaluated for several ions by spectrophotometric titrations in acetonitrile and acetonitrile/water. Compound **3a** was selective for the cyanide ion in ACN/H_2O (8:2), which is a very promising result as a colorimetric chemosensor for application in aqueous media.

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